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NEWS 1 Web Page for STN Seminar Schedule - N. America
NEWS 2 AUG 15 CAOLD to be discontinued on December 31, 2008
NEWS 3 OCT 07 EPFULL enhanced with full implementation of EPC2000
NEWS 4 OCT 07 Multiple databases enhanced for more flexible patent number searching
NEWS 5 OCT 22 Current-awareness alert (SDI) setup and editing enhanced
NEWS 6 OCT 22 WPIDS, WPINDEX, and WPIX enhanced with Canadian PCT Applications
NEWS 7 OCT 24 CHEMLIST enhanced with intermediate list of pre-registered REACH substances
NEWS 8 NOV 21 CAS patent coverage to include exemplified prophetic substances identified in English-, French-, German-, and Japanese-language basic patents from 2004-present
NEWS 9 NOV 26 MARPAT enhanced with FSORT command
NEWS 10 NOV 26 MEDLINE year-end processing temporarily halts availability of new fully-indexed citations
NEWS 11 NOV 26 CHEMSAFE now available on STN Easy
NEWS 12 NOV 26 Two new SET commands increase convenience of STN searching
NEWS 13 DEC 01 ChemPort single article sales feature unavailable
NEWS 14 DEC 12 GBFULL now offers single source for full-text coverage of complete UK patent families
NEWS 15 DEC 17 Fifty-one pharmaceutical ingredients added to PS

NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,
AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.

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STNsearch

FILE 'HOME' ENTERED AT 17:00:03 ON 31 DEC 2008

FILE 'REGISTRY' ENTERED AT 17:00:17 ON 31 DEC 2008
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STRUCTURE FILE UPDATES: 30 DEC 2008 HIGHEST RN 1092172-37-6
DICTIONARY FILE UPDATES: 30 DEC 2008 HIGHEST RN 1092172-37-6

New CAS Information Use Policies, enter HELP USAGETERMS for details.

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L1 STRUCTURE UPLOADED

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=> s 11
SAMPLE SEARCH INITIATED 17:03:30 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -          20 TO ITERATE
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100.0% PROCESSED 20 ITERATIONS 1 ANSWERS
SEARCH TIME: 00.00.01

| | | |
|------------------------|--------|--------------|
| FULL FILE PROJECTIONS: | ONLINE | **COMPLETE** |
| | BATCH | **COMPLETE** |
| PROJECTED ITERATIONS: | 132 TO | 668 |
| PROJECTED ANSWERS: | 1 TO | 80 |

L2 1 SEA SSS SAM L1

=> s 11

STNsearch

SAMPLE SEARCH INITIATED 17:03:34 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 20 TO ITERATE

100.0% PROCESSED 20 ITERATIONS 1 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 132 TO 668
PROJECTED ANSWERS: 1 TO 80

L3 1 SEA SSS SAM L1

=> s l1 full
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 185.40 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
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FULL SCREEN SEARCH COMPLETED - 288 TO ITERATE

100.0% PROCESSED 288 ITERATIONS 10 ANSWERS
SEARCH TIME: 00.00.01

L4 10 SEA SSS FUL L1

=> file hcplus
COST IN U.S. DOLLARS SINCE FILE TOTAL
SESSION
FULL ESTIMATED COST 188.28 188.50

FILE 'HCAPLUS' ENTERED AT 17:03:41 ON 31 DEC 2008
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FILE COVERS 1907 - 31 Dec 2008 VOL 150 ISS 1
FILE LAST UPDATED: 30 Dec 2008 (20081230/ED)

HCAplus now includes complete International Patent Classification (IPC) reclassification data for the third quarter of 2008.

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

STNsearch

=> s 14
L5 8 L4

=> s 15 and gasparini, f?/au
227 GASPARINI, F?/AU
L6 6 L5 AND GASPARINI, F?/AU

=> d 16, ibib abs hitstr, 1-6

L6 ANSWER 1 OF 6 HCPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:344699 HCPLUS
DOCUMENT NUMBER: 149:372770
TITLE: Radiation dosimetry and biodistribution of ¹¹C-ABP688 measured in healthy volunteers
AUTHOR(S): Treyer, Valerie; Streffler, Johannes; Ametamey, Simon M.; Bettio, Andrea; Blaeuenstein, Peter; Schmidt, Mark; Gasparini, Fabrizio; Fischer, Uta; Hock, Christoph; Buck, Alfred
CORPORATE SOURCE: PET Center, Division of Nuclear Medicine, University Hospital Zurich, Zurich, 8091, Switz.
SOURCE: European Journal of Nuclear Medicine and Molecular Imaging (2008), 35(4), 766-770
CODEN: EJNMA6; ISSN: 1619-7070
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English

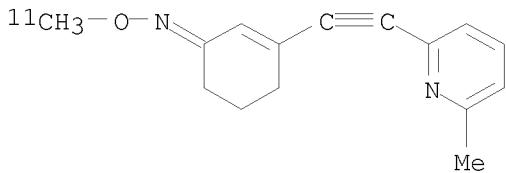
AB Introduction: In this study, we assessed the whole-body biodistribution and radiation dosimetry of the new glutamatergic ligand ¹¹C-ABP688. This ligand binds specifically to the metabotropic glutamatergic receptor of subtype 5 (mGluR5). Materials and methods: The study included five healthy male volunteers aged 20-29 years. After i.v. injection of 240-260 MBq, a series of four to ten whole-body positron emission tomog./computed tomog. scans were initiated, yielding 60-80 min of data. Residence times were then calculated in the relevant organs, and the software packages Mirdose and Olinda were used to calculate the absorbed radiation dose and the ED equivalent. Results: Of the excreted ¹¹C activity at 1 h, approx. 80% were eliminated via the hepato-biliary pathway and 20% through the urinary tract. The absorbed dose (mGy/MBq) was highest in the liver ($1.64 \times 10^{-2} \pm 5.08 \times 10^{-3}$), gallbladder ($8.13 \times 10^{-3} \pm 5.6 \times 10^{-3}$), and kidneys ($7.27 \times 10^{-3} \pm 2.79 \times 10^{-3}$). The ED equivalent was 3.68 ± 0.84 microSv/MBq. Brain uptake in the areas with high mGluR5 d. was 2-3 (SUV). The agreement between the values obtained from Mirdose and the Olinda was excellent. Conclusion: ¹¹C-ABP688 is a very promising ligand for the investigation of mGluR5 receptors in humans. Brain uptake is high and the ED equivalent so low that serial exams. in the same subject seem feasible.

IT 849469-02-9

RL: DGN (Diagnostic use); PKT (Pharmacokinetics); BIOL (Biological study);
USES (Uses)
(radiation dosimetry and biodistribution of ¹¹C-ABP688 measured in healthy volunteers)

RN 849469-02-9 HCPLUS

CN 2-Cyclohexen-1-one, 3-[2-(6-methyl-2-pyridinyl)ethynyl]-, O-(methyl-¹¹C)oxime (CA INDEX NAME)



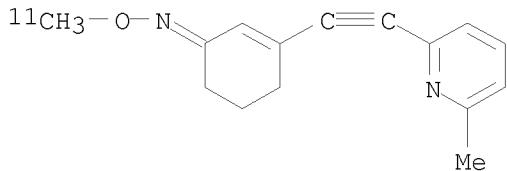
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 6 HCPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2007:1038614 HCPLUS
 DOCUMENT NUMBER: 147:497884
 TITLE: Evaluation of the metabotropic glutamate receptor subtype 5 using PET and ¹¹C-ABP688: assessment of methods
 AUTHOR(S): Treyer, Valerie; Streffer, Johannes; Wyss, Matthias T.; Bettio, Andrea; Ametamey, Simon M.; Fischer, Uta; Schmidt, Mark; Gasparini, Fabrizio; Hock, Christoph; Buck, Alfred
 CORPORATE SOURCE: PET Center, Division of Nuclear Medicine, University Hospital Zurich, Zurich, Switz.
 SOURCE: Journal of Nuclear Medicine (2007), 48(7), 1207-1215
 CODEN: JNMEAQ; ISSN: 0161-5505
 PUBLISHER: Society of Nuclear Medicine
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB ¹¹C-ABP688 is a new PET ligand to assess the subtype 5 metabotropic glutamate receptor (mGlu5). The purpose of this study was to evaluate different methods for the anal. of human ¹¹C-ABP688 data acquired from 6 healthy, young volunteers. The methods were a 1-tissue-compartment model (K₁, k_{2"}), a 2-tissue-compartment model (K₁-k₄), and the noncompartmental method developed by Logan. Parameters related to receptor d. were the total distribution volume (DV), DV" (= K₁/k_{2"}, 1 tissue compartment); specific DV, DVC2 (= K₁/k_{2'} + k_{3'}/k₄, 2 tissue compartments); and DVtot for the noncompartmental method. The 1-tissue-compartment model was too simple to adequately fit the data. DVC2 calculated with the 2-tissue-compartment model ranged from 5.45 ± 1.47 (anterior cingulate) to 1.91 ± 0.32 (cerebellum). The corresponding values for DVtot, calculated with the 2-tissue-compartment model and the Logan method (in parentheses), were 6.57 ± 1.45 (6.35 ± 1.32) and 2.93 ± 0.53 (2.48 ± 0.40). There was no clear evidence of a region devoid of mGlu5 receptors. The first-pass extraction fraction exceeded 95%. The minimal scan duration to obtain stable results was estimated to be 45 min. ¹¹C-ABP688 displays favorable kinetics for assessing mGlu5 receptors. For tracer kinetic modeling, 2-tissue-compartment models are clearly superior to models with only 1 tissue compartment. In comparison to the compartmental models, the Logan method is equally useful if only DVtot values are required and fast pixelwise parametric maps are desired. The lack of regions devoid of receptors limits the use of reference region methods that do not require arterial blood sampling. Another advantage of the tracer is the fast kinetics that allow for relatively short acquisitions.
 IT 849469-02-9
 RL: DGN (Diagnostic use); PKT (Pharmacokinetics); BIOL (Biological study); USES (Uses)

(assessment of methods for evaluation of metabotropic glutamate receptor subtype 5 using PET and ¹¹C-ABP688)

RN 849469-02-9 HCAPLUS

CN 2-Cyclohexen-1-one, 3-[2-(6-methyl-2-pyridinyl)ethynyl]-, O-(methyl-¹¹C)oxime (CA INDEX NAME)



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:346533 HCAPLUS

DOCUMENT NUMBER: 147:206659

TITLE: Human PET studies of metabotropic glutamate receptor subtype 5 with ¹¹C-ABP688

AUTHOR(S): Ametamey, Simon M.; Treyer, Valerie; Streffer, Johannes; Wyss, Matthias T.; Schmidt, Mark; Blagoev, Milen; Hintermann, Samuel; Auberson, Yves; Gasparini, Fabrizio; Fischer, Uta C.; Buck, Alfred

CORPORATE SOURCE: PSI, Center for Radiopharmaceutical Science of ETH, Zurich, Switz.

SOURCE: Journal of Nuclear Medicine (2007), 48(2), 247-252
CODEN: JNMEAQ; ISSN: 0161-5505

PUBLISHER: Society of Nuclear Medicine

DOCUMENT TYPE: Journal

LANGUAGE: English

AB 3-(6-Methyl-pyridin-2-ylethyynyl)-cyclohex-2-enone-O-¹¹C-methyl-oxime (¹¹C-ABP688), a noncompetitive and highly selective antagonist for the metabotropic glutamate receptor subtype 5 (mGluR5), was evaluated for its potential as a PET agent. Methods: Six healthy male volunteers (mean age, 25 y; range, 21-33 y) were studied. Brain perfusion (¹⁵⁰-H₂O) was measured immediately before each ¹¹C-ABP688 PET scan. For anat. coregistration, T1-weighted MRI was performed on each subject. Arterial blood samples for the determination of the arterial input curve were obtained

at

predefined time points, and ¹¹C-ABP688 uptake was assessed quant. using a 2-tissue-compartment model. Results: An initial rapid uptake of radioactivity followed by a gradual clearance from all examined brain regions was observed. Relatively high radioactivity concns. were observed in mGluR5-rich brain regions such as the anterior cingulate, medial temporal lobe, amygdala, caudate, and putamen, whereas radioactivity uptake in the cerebellum and white matter, regions known to contain low densities of mGluR5, was low. Specific distribution volume as an outcome measure of mGluR5 d. in the various brain regions ranged from 5.45 ± 1.47 (anterior cingulate) to 1.91 ± 0.32 (cerebellum), and the rank order of the corresponding specific distribution vols. of ¹¹C-ABP688 in cortical regions was temporal > frontal > occipital > parietal. The metabolism of

¹¹C-ABP688 in plasma was rapid; at 60 min after injection, 25% ± 0.03% of radioactivity measured in the plasma of healthy volunteers was intact parent compound Conclusion: The results of these studies indicate that ¹¹C-ABP688 has suitable characteristics and is a promising PET ligand for imaging mGluR5 distribution in humans. Furthermore, it could be of great value for the selection of appropriate doses of clin. relevant candidate drugs that bind to mGluR5 and for PET studies of patients with psychiatric and neurol. disorders.

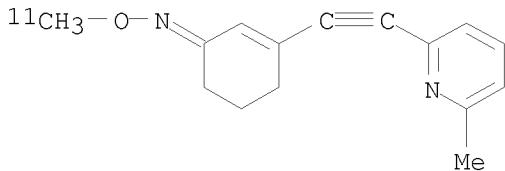
IT 849469-02-9

RL: DGN (Diagnostic use); PKT (Pharmacokinetics); BIOL (Biological study); USES (Uses)

(utility of ¹¹C-ABP688 for labeling metabotropic glutamate receptor subtype 5 distribution in human brain using PET)

RN 849469-02-9 HCPLUS

CN 2-Cyclohexen-1-one, 3-[2-(6-methyl-2-pyridinyl)ethynyl]-, O-(methyl-¹¹C)oxime (CA INDEX NAME)



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 6 HCPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:1331235 HCPLUS

DOCUMENT NUMBER: 146:223524

TITLE: ABP688, a novel selective and high affinity ligand for the labeling of mGlu5 receptors: Identification, *in vitro* pharmacology, pharmacokinetic and biodistribution studies

AUTHOR(S): Hintermann, Samuel; Vranesic, Ivo; Allgeier, Hans; Brue lisauer, Armin; Hoyer, Daniel; Lemaire, Michel; Moenius, Thomas; Urwyler, Stephan; Whitebread, Steven; Gasparini, Fabrizio; Auberson, Yves P.

CORPORATE SOURCE: Novartis Institutes for BioMedical Research, Basel, 4002, Switz.

SOURCE: Bioorganic & Medicinal Chemistry (2007), 15(2), 903-914

PUBLISHER: CODEN: BMECEP; ISSN: 0968-0896
Elsevier Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

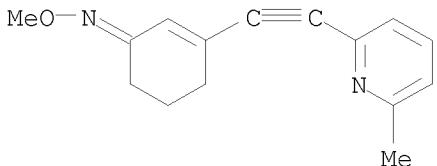
OTHER SOURCE(S): CASREACT 146:223524

AB [11C]ABP688 (2) has recently been demonstrated to be a useful PET tracer for *in vivo* imaging of the metabotropic glutamate receptors type 5 (mGluR5) in rodents. We describe here the identification and preclin. profiling of ABP688 and its tritiated version [³H]ABP688, and show that its high affinity ($K_d = 2$ nM), selectivity, and pharmacokinetic properties fulfill all requirements for development as a PET tracer for clin. imaging of the mGlu5 receptor.

IT 924298-51-1P, ABP 688

RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
 (ABP688 and [3H]ABP688 preparation and pharmacokinetics: ABP688 suitability for [11C] radiolabeling and use in PET imaging of mGlu5 receptors)

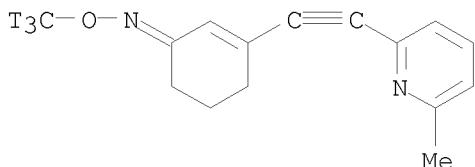
RN 924298-51-1 HCPLUS

CN 2-Cyclohexen-1-one, 3-[2-(6-methyl-2-pyridinyl)ethynyl]-, O-methyloxime
 (CA INDEX NAME)

IT 880302-34-1P, [3H]ABP 688

RL: PKT (Pharmacokinetics); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
 (ABP688 and [3H]ABP688 preparation and pharmacokinetics: ABP688 suitability for [11C] radiolabeling and use in PET imaging of mGlu5 receptors)

RN 880302-34-1 HCPLUS

CN 2-Cyclohexen-1-one, 3-[2-(6-methyl-2-pyridinyl)ethynyl]-, O-(methyl-t3)oxime
 (CA INDEX NAME)

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 6 HCPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:427101 HCPLUS

DOCUMENT NUMBER: 146:353694

TITLE: Radiosynthesis and preclinical evaluation of 11C-ABP688 as a probe for imaging the metabotropic glutamate receptor subtype 5

AUTHOR(S): Ametamey, Simon M.; Kessler, Lea J.; Honer, Michael; Wyss, Matthias T.; Buck, Alfred; Hintermann, Samuel; Auberson, Yves P.; Gasparini, Fabrizio; Schubiger, Pius A.

CORPORATE SOURCE: Department of Chemistry and Applied Biosciences of ETH, Center for Radiopharmaceutical Science of ETH, PSI and USZ, Zurich, Switz.

SOURCE: Journal of Nuclear Medicine (2006), 47(4), 698-705
 CODEN: JNMEAQ; ISSN: 0161-5505

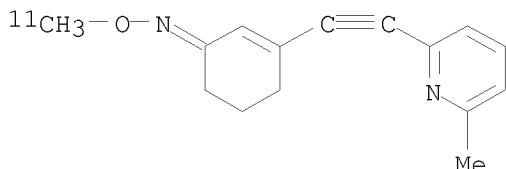
PUBLISHER: Society of Nuclear Medicine

DOCUMENT TYPE: Journal

LANGUAGE: English
 AB 11C-ABP688 (3-(6-methyl-pyridin-2-ylethynyl)-cyclohex-2-enone-0-11C-methyl-oxime), a noncompetitive and highly selective antagonist for the metabotropic glutamate receptor subtype 5 (mGluR5), was evaluated for its potential as a PET agent. ABP688 was radiolabeled with 11C by reacting 11C-Me iodide with the sodium salt of desmethyl-ABP688 (3-(6-methyl-pyridin-2-ylethynyl)-cyclohex-2-enone oxime). The affinity of 11C-ABP688 for mGluR5 was determined by Scatchard anal. using rat whole-brain membranes (without cerebellum). Ex vivo autoradiog., biodistribution, and PET studies with 11C-ABP688 were performed on rats, wild-type mice, and mGluR5-knock-out mice. The overall synthesis time was 45-50 min from the end of radionuclide production 11C-ABP688 was obtained in good radiochem. yield ($35\% \pm 8\%$, n = 17, decay corrected), and the specific radioactivity was 150 ± 50 GBq/ μ mol (n = 17) at the end of the synthesis. Scatchard anal. revealed a single high-affinity binding site with a dissociation constant of 1.7 ± 0.2 nmol/L and a maximum number of binding

sites of 231 ± 18 fmol/mg of protein. Ex vivo autoradiog. in wild-type mice and rats showed a heterogeneous distribution pattern consistent with the known distribution of mGluR5 in the brain, with the highest uptake in hippocampus, striatum, and cortex. Blocking studies by coinjection of 11C-ABP688 and unlabeled 2-methyl-6-(3-methoxyphenyl)ethynyl-pyridine (1 mg/kg), an antagonist for mGluR5, revealed up to 80% specific binding in rat brain. In mGluR5-knock-out mouse brain, a homogeneous and markedly reduced accumulation of 11C-ABP688 was observed. PET studies on rats and mice using a small-animal PET scanner also demonstrated radioactivity uptake in the brain regions known to be rich in mGluR5. In contrast, radioactivity uptake in mGluR5-knock-out mice was fairly uniform, substantiating the specificity of 11C-ABP688 binding to mGluR5. 11C-ABP688 is a selective tracer for imaging mGluR5 in vivo in rodents and may offer a future tool for imaging mGluR5 in humans using PET.

IT 849469-02-9P
 RL: DGN (Diagnostic use); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (radiosynthesis and preclin. evaluation of carbon-11-ABP688 as probe for imaging metabotropic glutamate receptor subtype 5)
 RN 849469-02-9 HCPLUS
 CN 2-Cyclohexen-1-one, 3-[2-(6-methyl-2-pyridinyl)ethynyl]-, O-(methyl-11C)oxime (CA INDEX NAME)



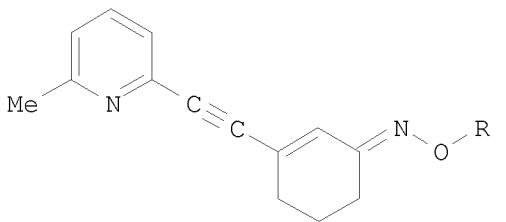
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 6 HCPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2005:300406 HCPLUS
 DOCUMENT NUMBER: 142:373688
 TITLE: A preparation of pyridylacetylene derivatives, useful

INVENTOR(S): as radiotracers and imaging agents
 Gasparini, Fabrizio; Auberson, Yves;
 Kessler, Lea; Ametamey, Simon Mensah
 PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
 SOURCE: PCT Int. Appl., 14 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|----------|------------------|------------|
| WO 2005030723 | A1 | 20050407 | WO 2004-EP10743 | 20040924 |
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CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
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EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
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SN, TD, TG | | | | |
| AU 2004275971 | A1 | 20050407 | AU 2004-275971 | 20040924 |
| AU 2004275971 | B2 | 20081002 | | |
| CA 2539469 | A1 | 20050407 | CA 2004-2539469 | 20040924 |
| EP 1670762 | A1 | 20060621 | EP 2004-765586 | 20040924 |
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IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK | | | | |
| CN 1856468 | A | 20061101 | CN 2004-80027309 | 20040924 |
| BR 2004014732 | A | 20061121 | BR 2004-14732 | 20040924 |
| JP 2007506698 | T | 20070322 | JP 2006-527359 | 20040924 |
| MX 2006PA03424 | A | 20060620 | MX 2006-PA3424 | 20060324 |
| IN 2006CN01019 | A | 20070629 | IN 2006-CN1019 | 20060324 |
| PRIORITY APPLN. INFO.: | | | GB 2003-22612 | A 20030926 |
| | | | WO 2004-EP10743 | W 20040924 |

OTHER SOURCE(S): CASREACT 142:373688; MARPAT 142:373688
 GI



AB The invention relates to novel pyridylacetylene derivs. of formula I [R is

Me, (CH₂)_{1-4I}, (CH₂)_{1-4Br}, (CH₂)_{1-4F}. or their labeled analog], useful as radiotracers and markers. For instance, pyridylacetylene derivative II (I, R = ¹¹CH₃) was prepared via methylation of I (R = H) by ¹¹CH₃I. The affinity for the mGlu5 receptor was determined using a radioligand displacement technique. II showed an IC₅₀ of 8 nM for the displacement of [³H]-2-methyl-6-[(3-methoxyphenyl)ethynyl]pyridine from membrane of L-tk cells stably expressing the human mGlu5 receptor.

IT 1044658-93-6

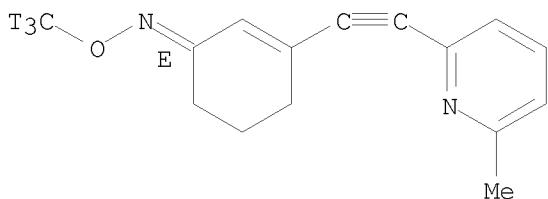
RL: PRPH (Prophetic)

(A preparation of pyridylacetylene derivatives, useful as radiotracers and imaging agents)

RN 1044658-93-6 HCPLUS

CN INDEX NAME NOT YET ASSIGNED

Double bond geometry as shown.

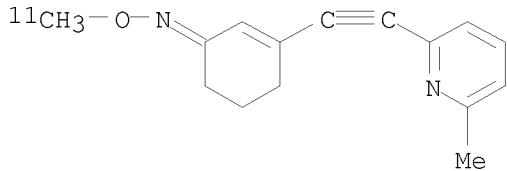


IT 849469-02-9P 849469-04-1P 849469-05-2P

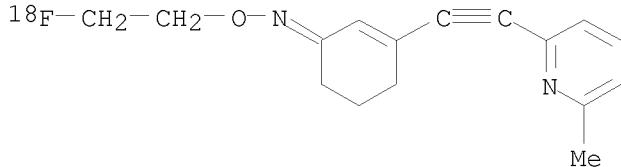
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of pyridylacetylene derivs. useful as radiotracers and imaging agents)

RN 849469-02-9 HCPLUS

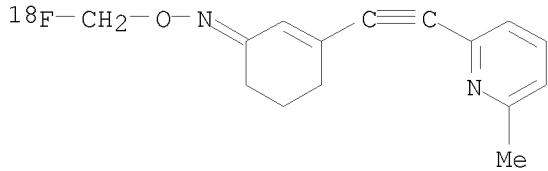
CN 2-Cyclohexen-1-one, 3-[2-(6-methyl-2-pyridinyl)ethynyl]-, O-(methyl-¹¹C)oxime (CA INDEX NAME)

RN 849469-04-1 HCPLUS

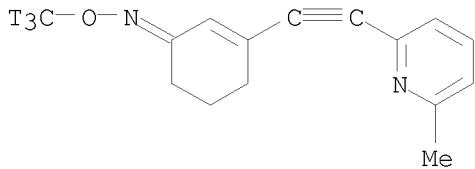
CN 2-Cyclohexen-1-one, 3-[2-(6-methyl-2-pyridinyl)ethynyl]-, O-[2-(fluoro-¹⁸F)ethyl]oxime (9CI) (CA INDEX NAME)

STNsearch

RN 849469-05-2 HCPLUS
CN 2-Cyclohexen-1-one, 3-[(6-methyl-2-pyridinyl)ethynyl]-,
O-(fluoro-18F-methyl)oxime (9CI) (CA INDEX NAME)



IT 880302-34-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of pyridylacetylene derivs. useful as radiotracers and imaging agents)
RN 880302-34-1 HCPLUS
CN 2-Cyclohexen-1-one, 3-[(6-methyl-2-pyridinyl)ethynyl]-, O-(methyl-t3)oxime
(CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 17:00:03 ON 31 DEC 2008)

FILE 'REGISTRY' ENTERED AT 17:00:17 ON 31 DEC 2008

L1 STRUCTURE uploaded
L2 1 S L1
L3 1 S L1
L4 10 S L1 FULL

FILE 'HCPLUS' ENTERED AT 17:03:41 ON 31 DEC 2008

L5 8 S L4
L6 6 S L5 AND GASPARINI, F?/AU

=> s 15 not 16
L7 2 L5 NOT L6

=> s 17 and auberson, y?/au
58 AUBERSON, Y?/AU
L8 0 L7 AND AUBERSON, Y?/AU

=> s 17 and kessler, l?/au

Updated Search

L9 147 KESSLER, L?/AU
1 L7 AND KESSLER, L?/AU

=> d 19, ibib abs hitstr, 1

L9 ANSWER 1 OF 1 HCPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:1290446 HCPLUS
DOCUMENT NUMBER: 149:121836
TITLE: Radiolabeling and in vitro and in vivo evaluation of [18F]-FE-DABP688 as a PET radioligand for the metabotropic glutamate receptor subtype 5
AUTHOR(S): Honer, Michael; Stoffel, Anja; Kessler, Lea J.; Schubiger, P. August; Ametamey, Simon M.
CORPORATE SOURCE: Animal Imaging Center - PET, Center for Radiopharmaceutical Science of ETH, PSI and USZ, ETH Hoenggerberg, Zurich, CH-8093, Switz.
SOURCE: Nuclear Medicine and Biology (2007), 34(8), 973-980
CODEN: NMBIEO; ISSN: 0969-8051

PUBLISHER: Elsevier Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Fluoroethyl-desmethyl-ABP688 (FE-DABP688) is a novel derivative of the previously described positron emission tomog. (PET) ligand 3-(6-methyl-pyridin-2-ylethynyl)-cyclohex-2-enone-O-[11C]-methyl-oxime. FE-DABP688 was radiolabeled with fluorine-18 and characterized as a PET imaging agent for the metabotropic glutamate receptor subtype 5 (mGluR5). FE-DABP688 was radiolabeled by reacting 2-[18F]-fluoroethyl tosylate with the sodium salt of 3-(pyridin-2-ylethynyl)-cyclohex-2-enone-oxime in dry DMF. The in vitro affinity of [18F]-FE-DABP688 for mGluR5 was determined by Scatchard anal. of saturation binding data using rat whole-brain membranes (without cerebellum). Further in vitro characterization of the tracer involved plasma stability and lipophilicity testing. In vivo evaluation of [18F]-FE-DABP688 was performed by postmortem biodistribution expts. and PET studies in rats using the dedicated small-animal PET tomograph quad-HIDAC. The radiotracer was obtained in good radiochem. yields in an overall synthesis time of 150 min. The radiochem. yield after semipreparative HPLC was 25±8% (n > 7, decay corrected), and specific activity was 30 ± 5 GBq/µmol (n>7). [18F]-FE-DABP688 exhibited optimal lipophilicity with a logD value of 2.1 ± 0.1 and high plasma stability. Saturation assays of [18F]-FE-DABP688 revealed a single high-affinity binding site with a dissociation constant (Kd) of 1.6 ± 0.4 nM and a Bmax value of 119 ± 24 fmol/mg protein. PET scanning indicated radioactivity uptake in mGluR5-rich regions such as the hippocampus, striatum and cortex, while radioactivity accumulation in the cerebellum, a region with negligible mGluR5 d., was significantly lower. Biodistribution studies showed a similar distribution pattern of [18F]-FE-DABP688 binding in the brain. The hippocampus-to-cerebellum and striatum-to-cerebellum ratios were 1.81 ± 0.16 and 1.93 ± 0.36, resp. Blocking studies using coinjection of [18F]-FE-DABP688 and unlabeled 2-methyl-6-((3-methoxyphenyl)ethynyl)-pyridine (1 mg/kg) revealed more than 45% specific binding in the hippocampus and striatum, thus demonstrating the in vivo specificity of tracer binding. [18F]-FE-DABP688 may be a useful PET tracer for imaging mGluR5 in rodents.

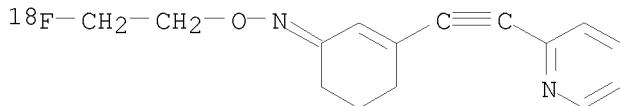
IT 1036752-38-1P
RL: DGN (Diagnostic use); PKT (Pharmacokinetics); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)

STNsearch

(radiolabeling and evaluation of [18F]-FE-DABP688 as PET radioligand
for mGluR5)

RN 1036752-38-1 HCAPLUS

CN 2-Cyclohexen-1-one, 3-[2-(2-pyridinyl)ethynyl]-,
O-[2-(fluoro-18F)ethyl]oxime (CA INDEX NAME)



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 17:00:03 ON 31 DEC 2008)

FILE 'REGISTRY' ENTERED AT 17:00:17 ON 31 DEC 2008

L1 STRUCTURE UPLOADED

L2 1 S L1

L3 1 S L1

L4 10 S L1 FULL

FILE 'HCAPLUS' ENTERED AT 17:03:41 ON 31 DEC 2008

L5 8 S L4

L6 6 S L5 AND GASPARINI, F?/AU

L7 2 S L5 NOT L6

L8 0 S L7 AND AUBERSON, Y?/AU

L9 1 S L7 AND KESSLER, L?/AU

=> s 15 not 19

L10 7 L5 NOT L9

=> s 17 not 19

L11 1 L7 NOT L9

=> s l11 and ametamey, s?/au

62 AMETAMEY, S?/AU

L12 0 L11 AND AMETAMEY, S?/AU

=> d l11, ibib abs hitstr, 1

L11 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:167983 HCAPLUS

DOCUMENT NUMBER: 134:222706

TITLE: Preparation of heterocyclic compounds as metabotropic glutamate receptor 5 (mGluR5) modulators

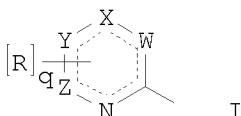
INVENTOR(S): Cosford, Nicholas D. P.; McDonald, Ian A.; Bleicher, Leo Solomon; Cube, Rowena V.; Schweiger, Edwin J.; Vernier, Jean-Michel; Hess, Stephen D.; Varney, Mark A.; Munoz, Benito

PATENT ASSIGNEE(S): Merck & Co., Inc., USA

SOURCE: PCT Int. Appl., 132 pp.
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 5
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|----------|-----------------|-------------|
| WO 2001016121 | A1 | 20010308 | WO 2000-US23923 | 20000831 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 6956049 | B1 | 20051018 | US 1999-387135 | 19990831 |
| CA 2383524 | A1 | 20010308 | CA 2000-2383524 | 20000831 |
| EP 1214303 | A1 | 20020619 | EP 2000-957932 | 20000831 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | | |
| JP 2003508390 | T | 20030304 | JP 2001-519688 | 20000831 |
| AU 780009 | B2 | 20050224 | AU 2000-69482 | 20000831 |
| PRIORITY APPLN. INFO.: | | | US 1999-387073 | A2 19990831 |
| | | | US 1999-387135 | A2 19990831 |
| | | | WO 2000-US23923 | W 20000831 |

OTHER SOURCE(S): MARPAT 134:222706
 GI



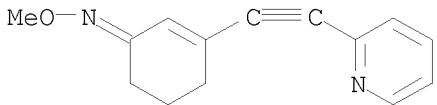
AB The title compds. I [ALB; A = 5-7 membered ring II (wherein at least one of W, X, Y and Z = (CR)p; p = 0-2, and the remainder of W, X, Y and Z = O, N, S; R = halo, (un)substituted aryl, heterocyclyl, etc.); L = (un)substituted alkenylene, alkynylene, azo; B = (un)substituted alkyl, cycloalkyl, heterocyclyl, etc.] and their pharmaceutically acceptable salts which are capable of modulating the activity of excitatory amino acid receptors such as metabotropic glutamate receptor, were prepared. Thus, reacting 2-bromo-1,3-thiazole with phenylacetylene in the presence of CuI, Et3N and PdCl2(PPh3)2 in DME followed by treatment of the resulting 2-(phenylethynyl)-1,3-thiazole with p-TsOH afforded 2-(phenylethynyl)-1,3-thiazole, p-TsOH salt which showed IC50 of 0.1 nM - 10 μM in Ca+2 flux assay and analgesic efficacy in analgesic animal model (CFA model).

IT 329204-51-5P 329204-53-7P 329204-55-9P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of heterocyclic compds. as metabotropic glutamate receptor 5
 (mGluR5) modulators)

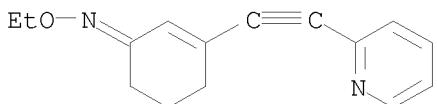
RN 329204-51-5 HCPLUS

CN 2-Cyclohexen-1-one, 3-[2-(2-pyridinyl)ethynyl]-, O-methyloxime (CA INDEX
 NAME)



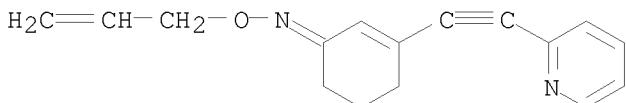
RN 329204-53-7 HCPLUS

CN 2-Cyclohexen-1-one, 3-[2-(2-pyridinyl)ethynyl]-, O-ethyloxime (CA INDEX
 NAME)



RN 329204-55-9 HCPLUS

CN 2-Cyclohexen-1-one, 3-[2-(2-pyridinyl)ethynyl]-, O-2-propen-1-yloxime (CA
 INDEX NAME)



REFERENCE COUNT:

9

THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> file caold

COST IN U.S. DOLLARS

| SINCE FILE
ENTRY | TOTAL
SESSION |
|---------------------|------------------|
|---------------------|------------------|

FULL ESTIMATED COST

56.52

245.02

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

| SINCE FILE
ENTRY | TOTAL
SESSION |
|---------------------|------------------|
|---------------------|------------------|

CA SUBSCRIBER PRICE

-6.56

-6.56

FILE 'CAOLD' ENTERED AT 17:06:13 ON 31 DEC 2008

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FILE COVERS 1907-1966

FILE LAST UPDATED: 01 May 1997 (19970501/UP)

STNsearch

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

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This file supports REGISTRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

CAOLD will be discontinued and removed from associated database clusters.

- . November 22, 2008 - removed from database clusters
- . December 31, 2008 - removed from STN

Content previously available only in CAOLD is now available in CA/CAplus. To learn more about the options available for transferring saved search queries and answer sets to CA/CAplus, contact your STN Service Center.

=> d his

(FILE 'HOME' ENTERED AT 17:00:03 ON 31 DEC 2008)

FILE 'REGISTRY' ENTERED AT 17:00:17 ON 31 DEC 2008

L1 STRUCTURE UPLOADED
L2 1 S L1
L3 1 S L1
L4 10 S L1 FULL

FILE 'HCAPLUS' ENTERED AT 17:03:41 ON 31 DEC 2008

L5 8 S L4
L6 6 S L5 AND GASPARINI, F?/AU
L7 2 S L5 NOT L6
L8 0 S L7 AND AUBERSON, Y?/AU
L9 1 S L7 AND KESSLER, L?/AU
L10 7 S L5 NOT L9
L11 1 S L7 NOT L9
L12 0 S L11 AND AMETAMEY, S?/AU

FILE 'CAOLD' ENTERED AT 17:06:13 ON 31 DEC 2008

=> s 14
L13 0 L4

=>

=> file regt
'REGT' IS NOT A VALID FILE NAME
SESSION CONTINUES IN FILE 'CAOLD'
Enter "HELP FILE NAMES" at an arrow prompt (=>) for a list of files

STNsearch

that are available. If you have requested multiple files, you can specify a corrected file name or you can enter "IGNORE" to continue accessing the remaining file names entered.

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=> file reg
COST IN U.S. DOLLARS          SINCE FILE      TOTAL
                                ENTRY        SESSION
FULL ESTIMATED COST          0.07          245.09
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE      TOTAL
                                                ENTRY        SESSION
CA SUBSCRIBER PRICE          0.00          -6.56
```

FILE 'REGISTRY' ENTERED AT 17:06:26 ON 31 DEC 2008
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 30 DEC 2008 HIGHEST RN 1092172-37-6
DICTIONARY FILE UPDATES: 30 DEC 2008 HIGHEST RN 1092172-37-6

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TSCA INFORMATION NOW CURRENT THROUGH July 5, 2008.

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REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stndoc/properties.html>

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=>
Uploading C:\Documents and Settings\brobinsone\My Documents\bbb.g.str
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L14 STRUCTURE UPLOADED

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=> s 114
SAMPLE SEARCH INITIATED 17:07:55 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -          3 TO ITERATE
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100.0% PROCESSED 3 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

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FULL FILE PROJECTIONS: ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:    3 TO      163
PROJECTED ANSWERS:       0 TO      0
```

L15 0 SEA SSS SAM L14

Updated Search

STNsearch

=> s 114 full
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 185.40 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 17:07:59 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 66 TO ITERATE

100.0% PROCESSED 66 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

L16 0 SEA SSS FUL L14

=>
Uploading C:\Documents and Settings\brobinson1\My Documents\arararar.str

L17 STRUCTURE UPLOADED

=> s 117
SAMPLE SEARCH INITIATED 17:09:12 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 2 TO ITERATE

100.0% PROCESSED 2 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 2 TO 124
PROJECTED ANSWERS: 0 TO 0

L18 0 SEA SSS SAM L17

=> s 117 full
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 185.40 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 17:09:16 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 45 TO ITERATE

100.0% PROCESSED 45 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

L19 0 SEA SSS FUL L17

Updated Search